Improving Adherence for Dyslipidemia and Anticoagulation

SMART

Stanford Medical Adherence Research Trial

Project Overview and Preliminary Results

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10/9/03

Project Objectives

- *The project seeks to improve the medication adherence and clinical control of ambulatory patients prescribed chronic oral treatment for two clinical situations:*
  - (1) HMG CoA reductase inhibitors (**statins**) for dyslipidemia
  - (2) Oral anticoagulation therapy with **warfarin** for thromboembolism

Background

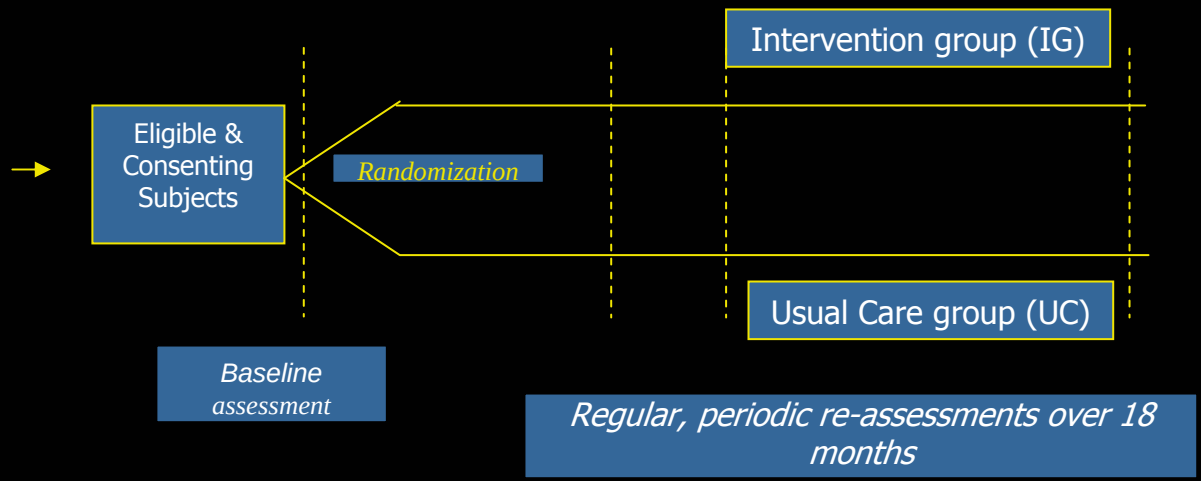
- *Conditions*
  - high prevalence
  - considerable long-term risk
  - well defined and established therapies
  - demonstrable benefit > risk
  - disappointing overall impact in real world settings
  - different enough to assess generalizability

- *Improving adherence*
  - better clinical outcomes
  - lessons useful for other conditions requiring long-term treatment with oral medications without prompts from symptoms

Issues Addressed

- The project is a randomized controlled trial that
  - *applies adherence-enhancing interventions*
    - Patient
    - Physician
    - Medical care system
  - *demonstrates improved levels of medication adherence*
    - Intervention Group vs. Usual Care Group
  - *evaluates the potential for dissemination*
    - academic clinic settings --> community-based practices
  - *assesses cost-effectiveness*
    - Intervention vs. usual care
    - Academic vs. community practice environments

Research Design



The project consists of two linked randomized controlled trials of interventions versus usual care, each over 18 months: a **confirmation phase** (Phase I) in an academic setting and a subsequent **dissemination phase** (Phase II) in diverse community settings.

Principal Hypotheses

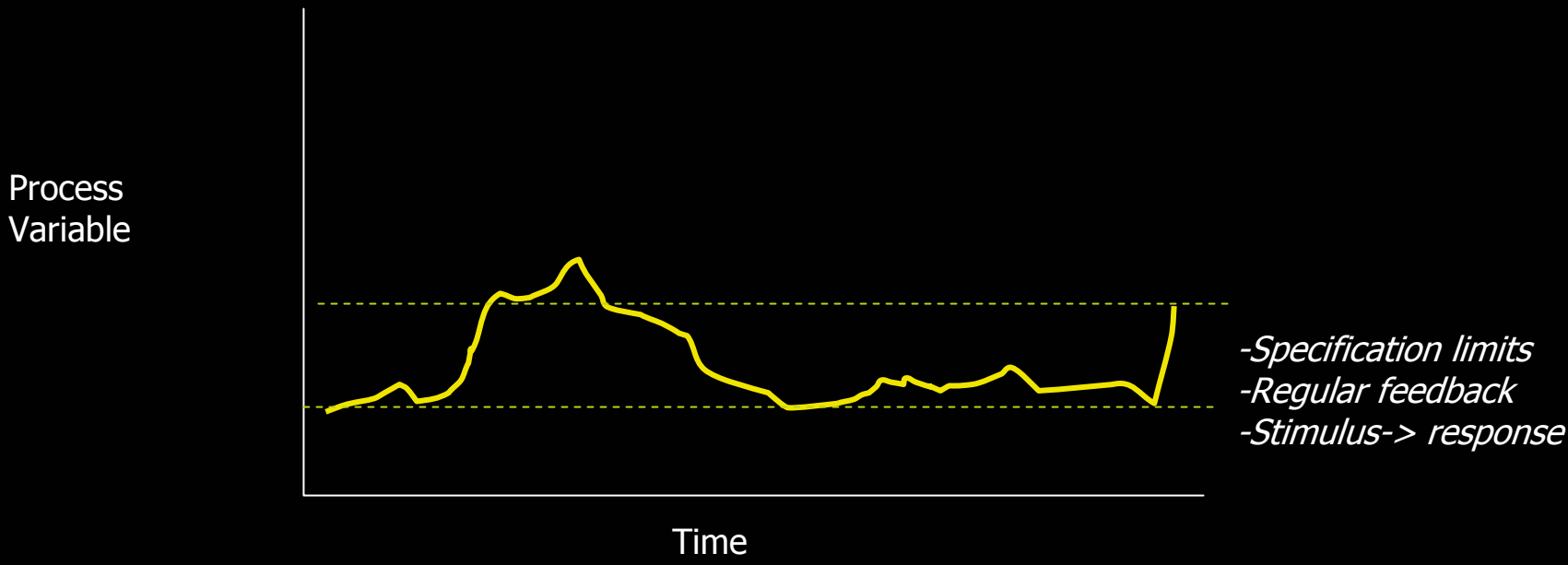
- *The **primary hypothesis** is that*
  - the integrated interventions --> significantly higher levels of days with correct dosings compared to usual care.

- *The **secondary hypotheses** are that*
  - (1) enhanced adherence --> improved clinical control
  - (2) the interventions can transition to community-based practice environments

Theoretical Basis

- ***Interventions***
  - Social cognitive and self-determination theory
  - Continuous quality improvement strategies
- ***Electronic medication monitoring (eDEM, AARDEX)***
  - Dynamic assessment of medication adherence
  - Correlation to clinical visits and test results
- ***Feedback about patient behavior***
  - Patients' achievements by levels of adherence and clinical control
  - Guides actions by the prescribing physician and the project educator.
- ***Feedback about physicians' behavior***
  - Adherence to practice guidelines
  - Improving overall adherence and outcomes.

CQI Model


Process
Variable
Time
-Specification limits
-Regular feedback
-Stimulus-> response

Inclusions & Exclusions

- **Patient Inclusion Criteria:**
  - *(a) age 21-79*
  - *(b) prescribed target medication(s) (warfarin or lovastatin, pravastatin, fluvastatin, simvastatin, or atorvastatin) for 18 months*
  - *(c) living or working within 30 minutes drive of Stanford*
  - *(d) fluent in spoken and written English*
  - *(e) provide written informed consent*

- **Patient Exclusion Criteria:**
  - *(a) inability to open and use electronic medication monitor vials without assistance;*
  - *(b) unwillingness to participate in study interventions or use the eDEM device*

Independent & Dependent Variables

Independent Variables	***Mediating Variables***	***Dependent Variables***
Sociodemographic Psychosocial Clinical Utilization Complications Major life events	Intervention vs. Usual Care Self-monitoring Feedback Alerts and reminders Academic detailing intensity	Days with proper dosing of target medication Change scores for clinical control (LDL cholesterol; proportion of days with therapeutic INR)

Project Operations

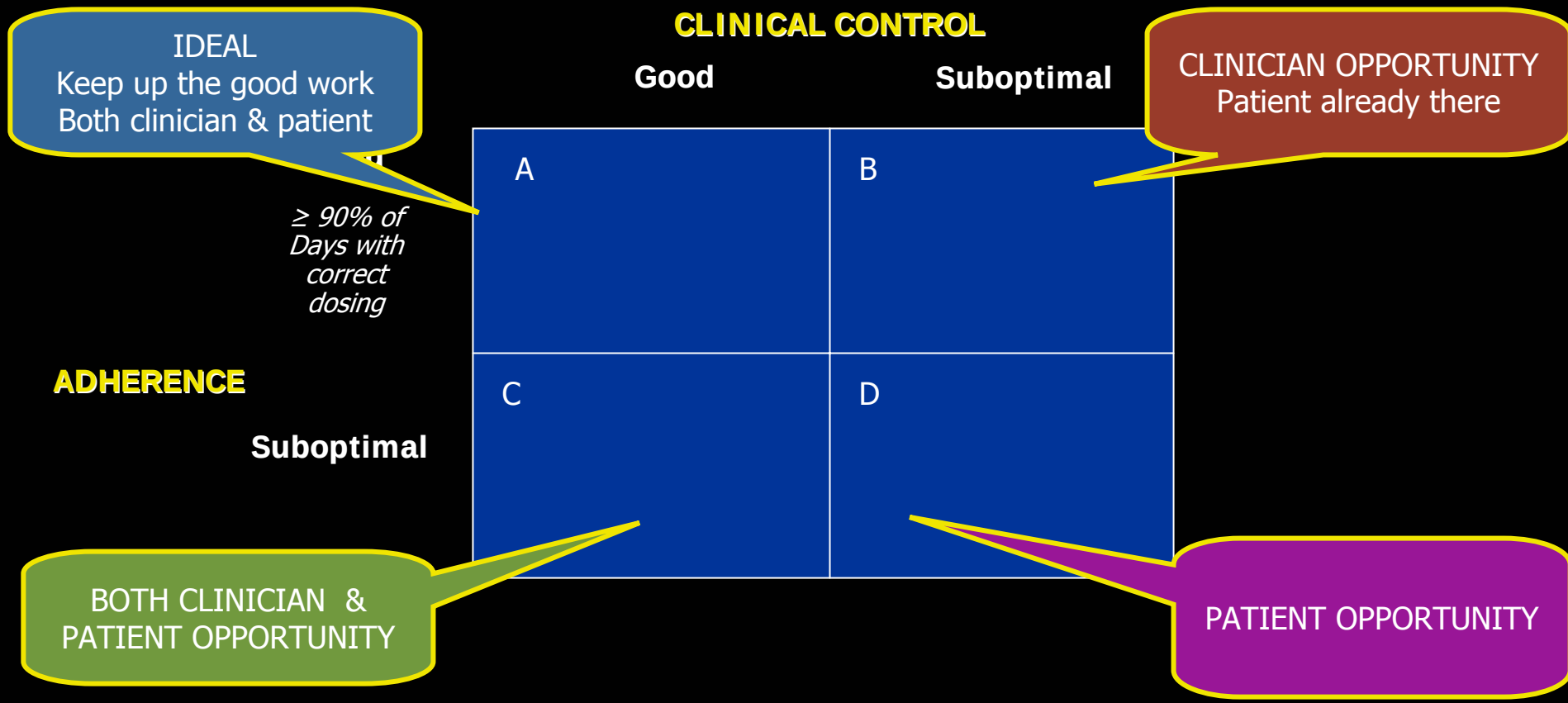
- Logistics
  - Patient self-report, self-monitoring diary
  - eDEM (Aardex) electronic medication monitor
  - Medical record review
  - Periodic reports to Intervention Group patients and physicians
  - 1-on-1 sessions
  - group sessions for academic detailing

- Adherence Measures
  - eDEM for medication-taking
  - Medical Record notes for physician changes

Preliminary Results (1)

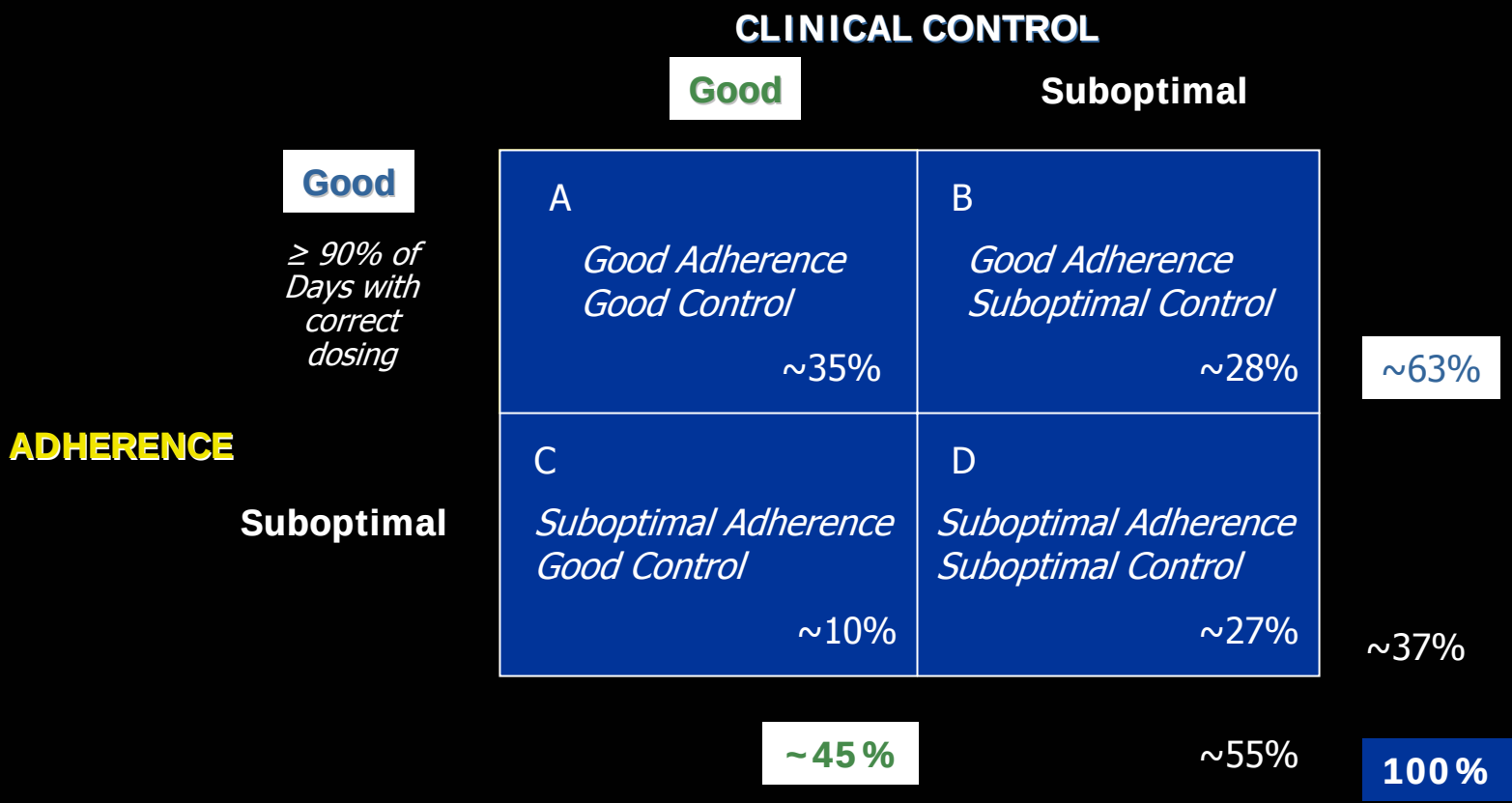
- Phase 1 (model confirmation)
  - *Recruitment 131 subjects (100% goal)*
    - 99 (76%) completed 18 month project with all data points
    - Dropouts 32 (24%)
      - *12 declined to continue*
      - *7 stopped study drug*
      - *3 moved*
      - *3 lost insurance*
      - *3 changed to non-study MDs*
      - *3 medical complications*
      - *1 death unrelated to study*

Matrix Model



Adapted from Sackett D: Hypertension in the real world: Public reaction, physician response, and patient compliance. In: Genest J, Koiw E, Kuchel O, eds. Hypertension: Physiopathology and Treatment. New York: McGraw-Hill, 1979; 1142-9.

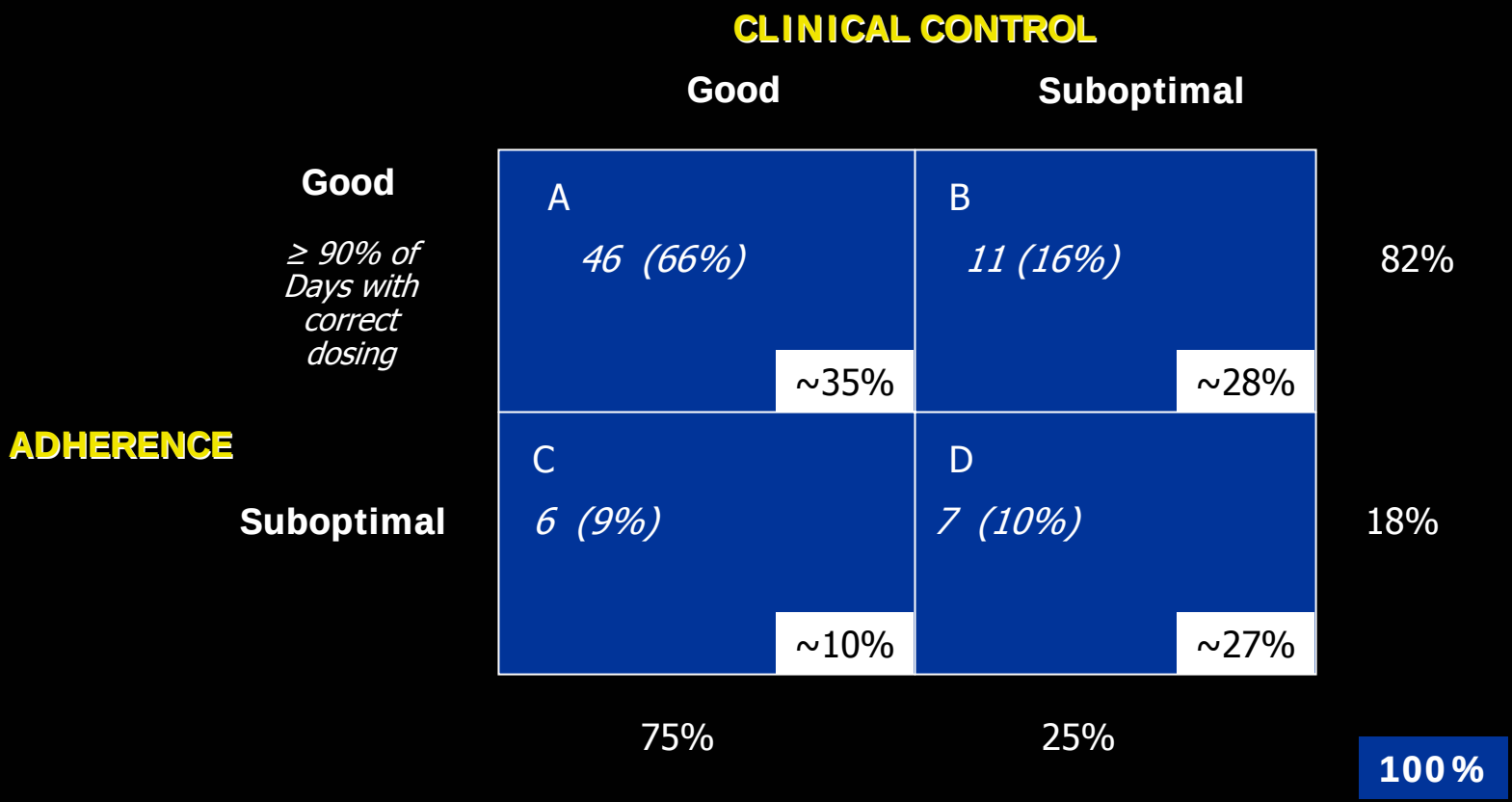
Matrix Model



Sackett DL, et al.: Compliance. Clinical Epidemiology; A Basic Science for Clinical Medicine. Boston: Little, Brown & Co, 1985; 199-222.
Silas J, et al.: Drug resistance, inappropriate dosing and non-compliance in hypertensive patients. Br J Clin Pharmacol 1980; 9: 427-30.

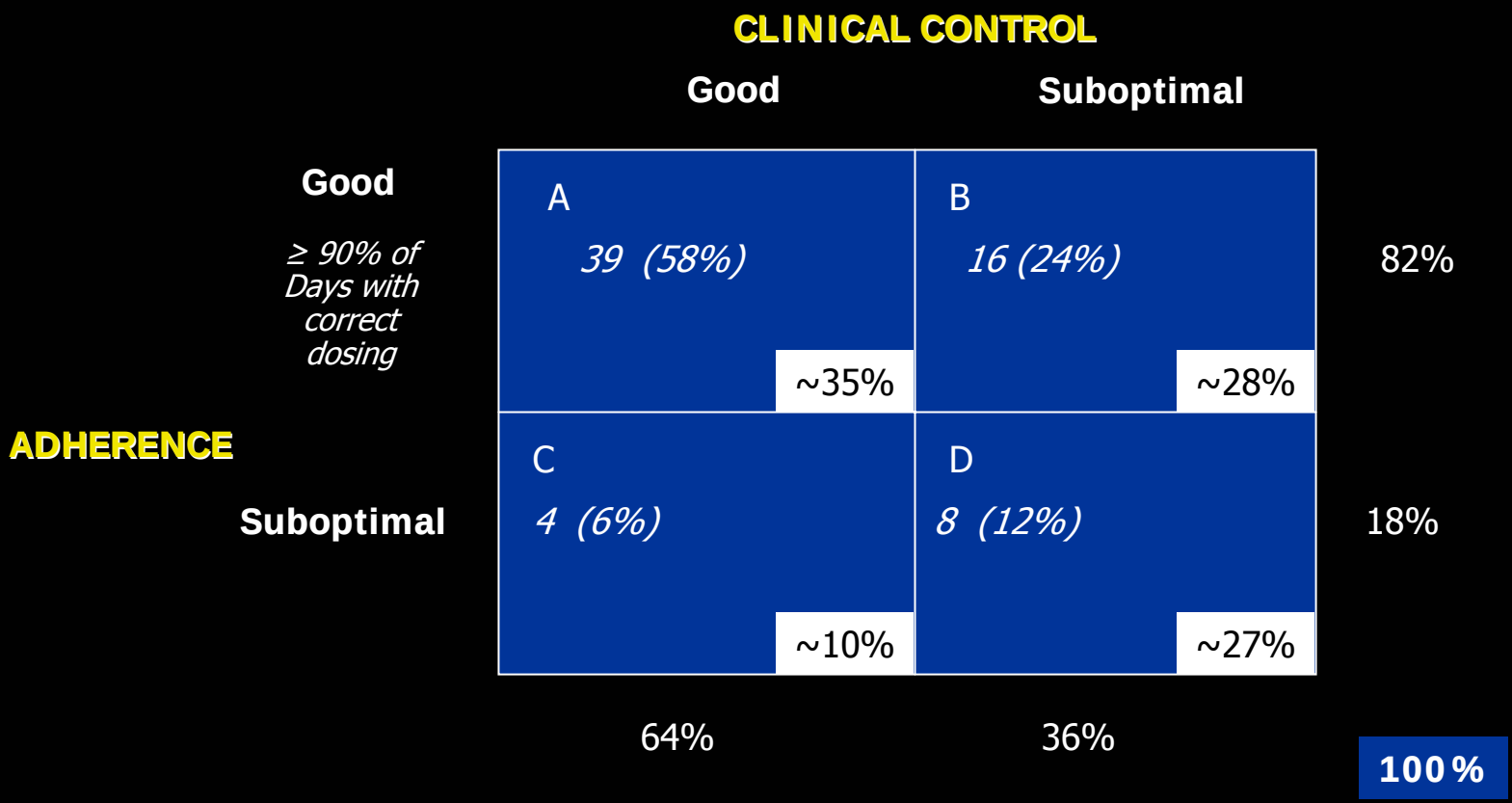
Matrix Results at 6 Months

Phase 1; Patients on statin therapy only



Matrix Results at 12 Months

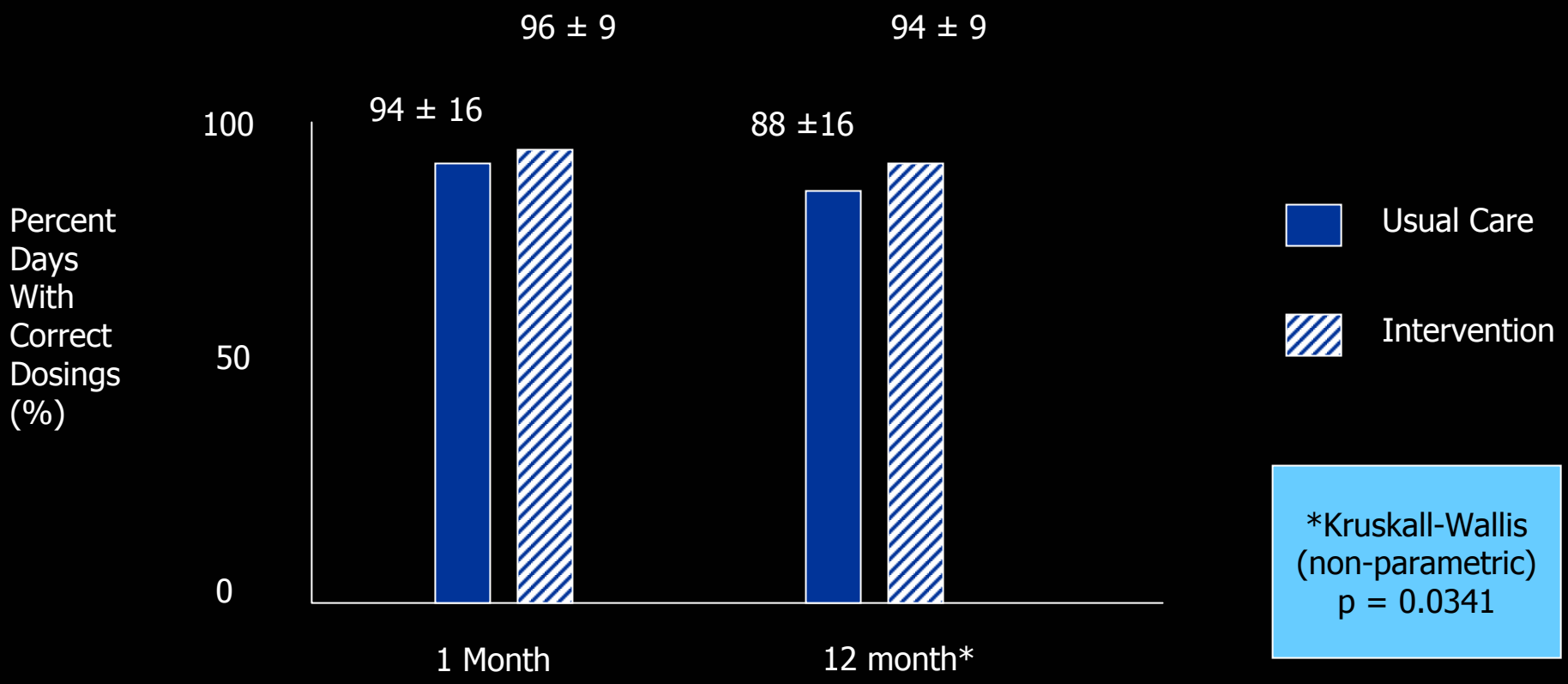
Phase 1; Patients on statin therapy only



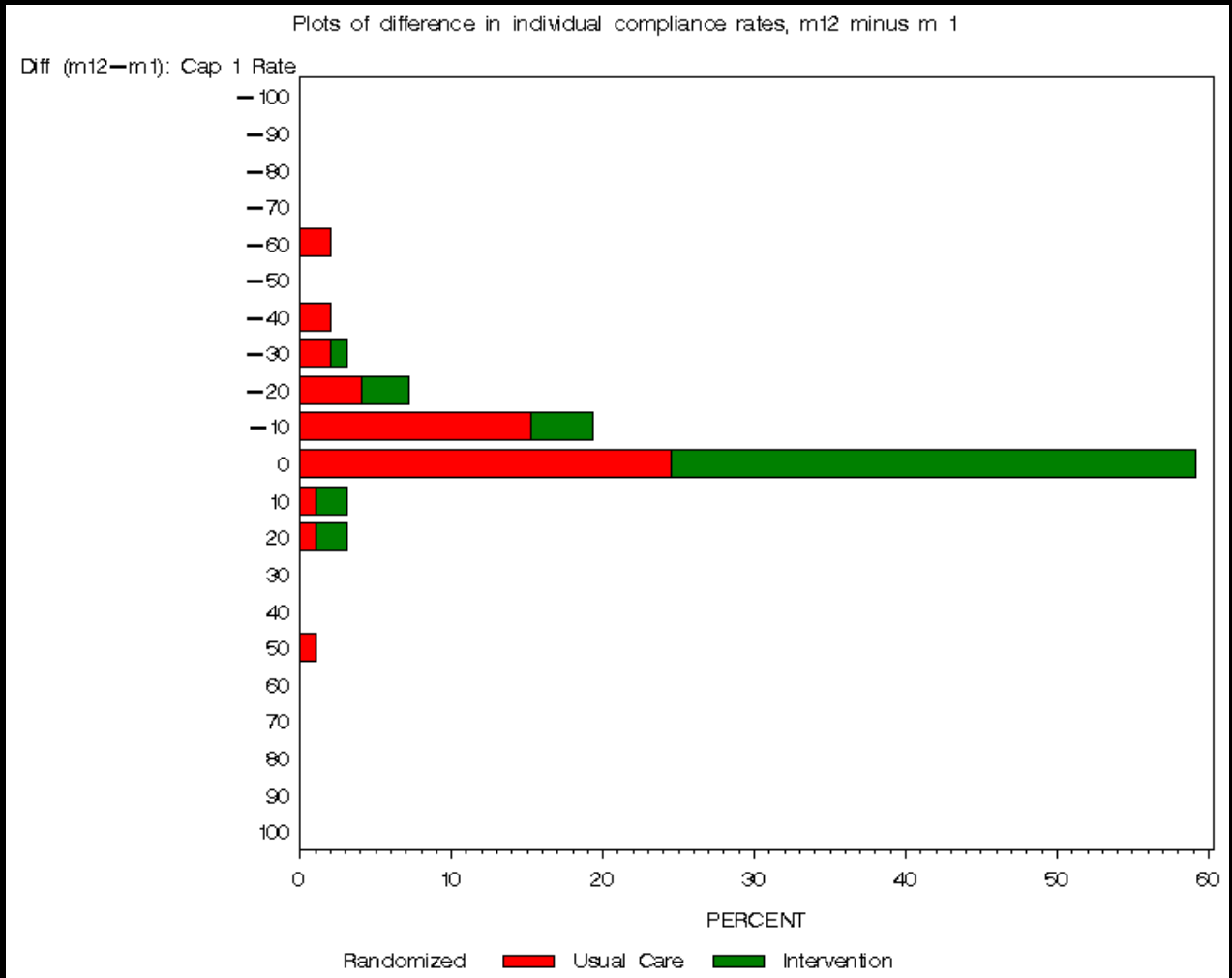
Phase 1 Results

- Highly adherent cohorts
- Well controlled with limited opportunity for improvement

Phase 1 Adherence

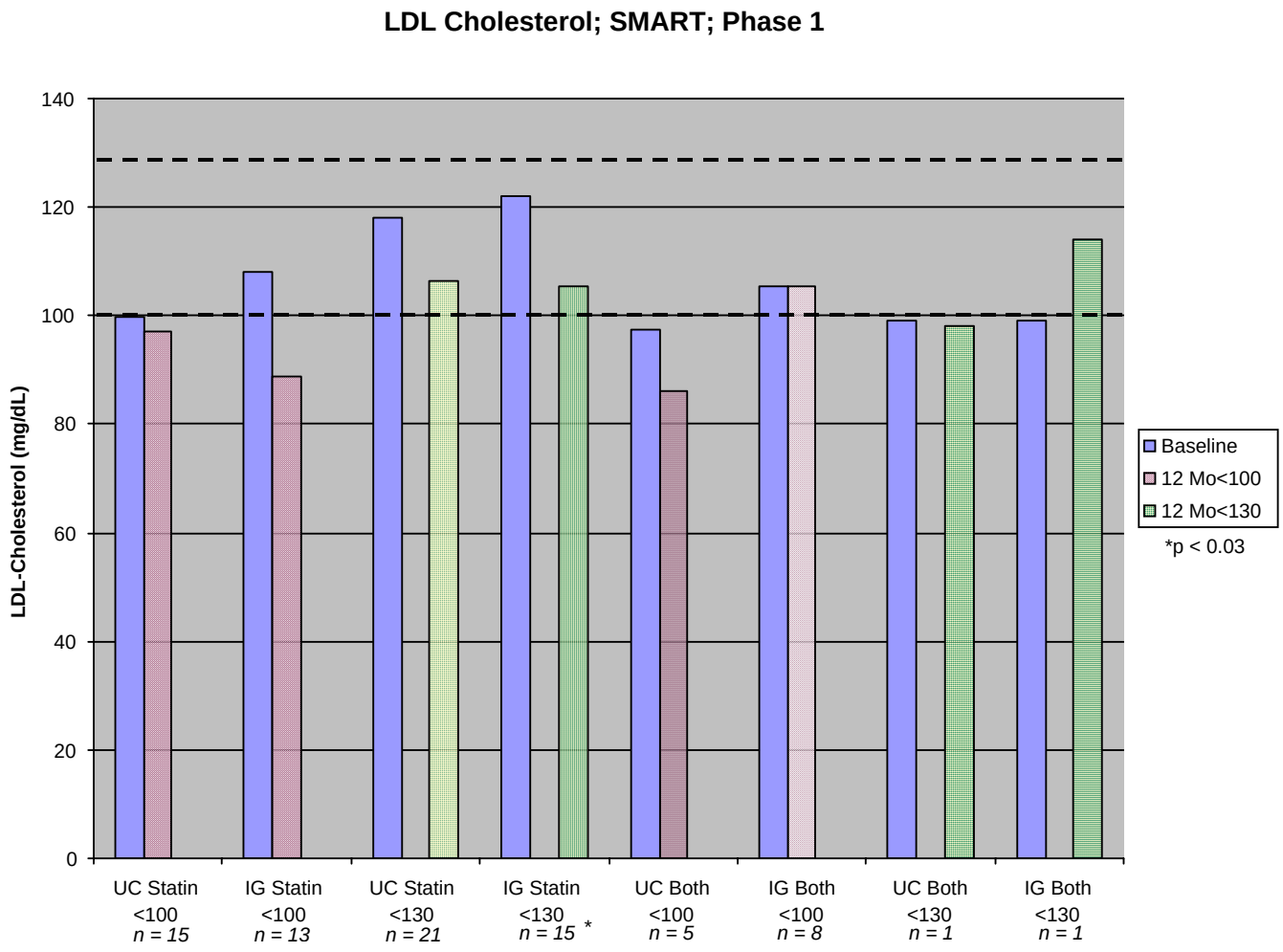


Changes in Adherence



CHANGE SCORES	Usual Care *n=52*	Intervention Group *n=46*
	-7.9±16.9	-1.5±8.5
5%	-41.4	-18.9
50%	-3.5	-0.7
95%	6.5	14.5

Changes in LDL Cholesterol
Phase 1



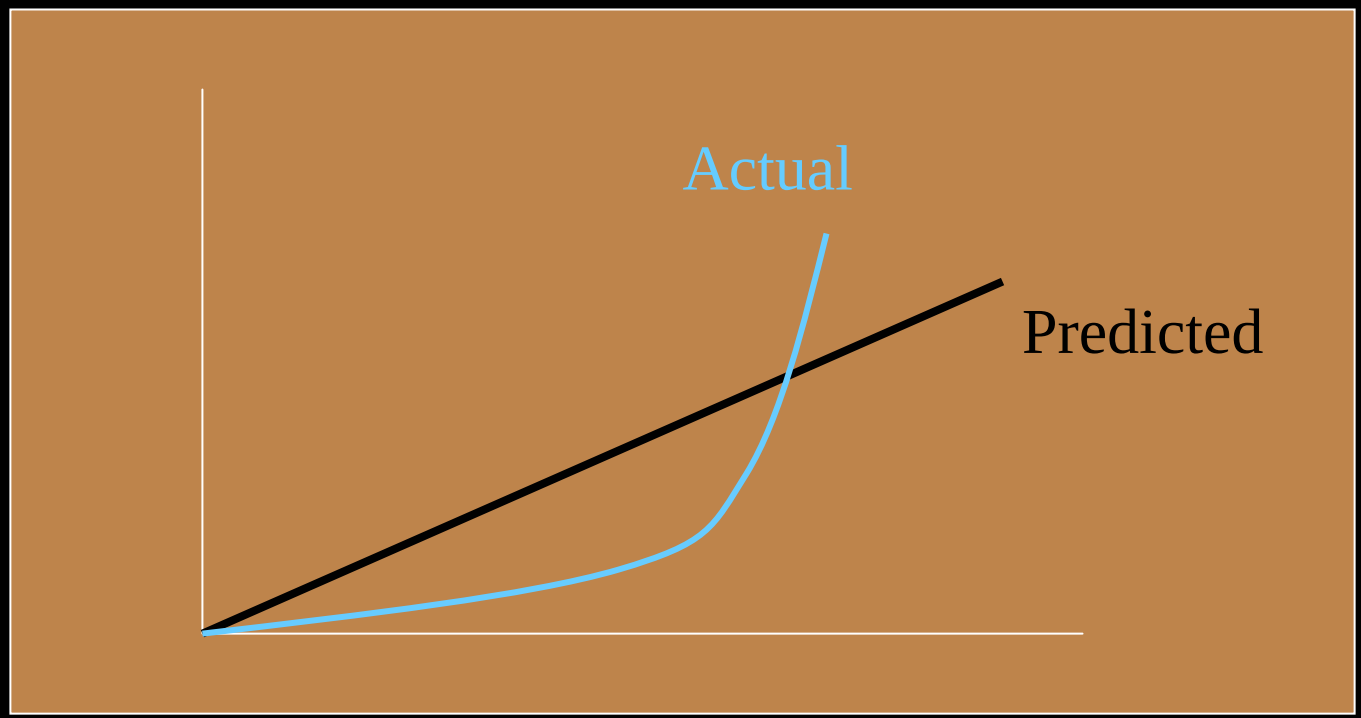
LDL-Cholesterol - Phase 1

	Baseline mg/dL	12 Month mg/dL	Change mg/dL
Usual Care (n = 40)	108.7 ± 7.5	100.1 ± 5.3	-10.7 ± 8.1
Intervention Group (n = 37)	107.3 ± 5.7	99.8 ± 4.2	-7.5 ± 5.1
			N.S (p >0.7)

Estimating Change

"We tend to overestimate change in the short run and underestimate it in the long run."

-Bill Gates



Adapted from MH Ebell; PQE Conference, 5/99

Summary

- Project: RCT in two phases for improving adherence among ambulatory patients with dyslipidemia and/or oral anticoagulation
- Theoretical basis from social cognitive, self-determination, and CQI methods
- Interventions aimed for PATIENT, PHYSICIAN, and SYSTEM
- Phase 1 (model confirmation)
    - Successful recruitment and retention to goals
    - High overall adherence; improved maintenance with intervention
- Matrix model suggests dynamic movement; opportunities for all
- Next challenges
    - Phase 2 recruitment under HIPAA
    - Acceptable and effective impact on physicians' adherence to guidelines
    - Data analysis for predictors of success (patient, physician, system) and dynamic patterns of adherence and control